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HPV Vaccine Is Weapon Against Cervical Ca

We may soon be able to prevent cervical cancer in women by vaccinating preteens against human papillomavirus.

Two candidate HPV vaccines—GlaxoSmithKline's Cervarix and Merck's Gardasil—are expected to be licensed for use in the United States in 2006. Both vaccines are highly effective in preventing infection with both HPV strains 16 and 18, which are responsible for 70%-75% of cervical cancers in women.

The Advisory Committee on Immunization Practices of the Centers for Disease Control and Prevention is already working on guidelines for their use, as is the American Academy of Pediatrics. Both groups are likely to recommend that the vaccines be given to girls aged 11-12 as part of the adolescent "vaccine platform," along with the meningococcal conjugate vaccine and the adolescent and adult DTaP vaccine.

I see this as a new frontier. It's a fabulous opportunity for those of us who work in vaccinology to be able to move from the prevention of infectious disease per se to the prevention of cancer. Cervical cancer affects approximately 12,000 women in the United States. And despite advances in Pap screening and treatment, the disease kills more than 4,000 women annually.

Nearly all (99.7%) of cervical cancer cases are caused by HPV infection. Approximately 15-20 of the 30-40 anogenital types of HPV that have been identified are oncogenic: HPV 16 causes about 54% of cases, and HPV 18 about 13%. Among the nononcogenic types, HPV 6 and 11 are most often associated with external genital warts. The Merck vaccine targets those two strains as well.

We know that acquisition of HPV typically occurs very soon after initiation of sexual intercourse. In a study of 608 U.S. college women who were followed at 6-month intervals, 43% had become infected with HPV by the third year. Indeed, nearly three-fourths of new HPV infections occur in sexually active young adults aged 15-24, and the prevalence of infection in women less than 25 years of age ranges from 28% to 46%.

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'It makes one wonder how much of our obesity problem and the emergence of metabolic syndrome in children may be the result of sleep deprivation.'

Dr. William G. Wilkoff, p. 27

As more vaccines are being added to the already-crowded childhood and adolescent immunization schedules, payers will be looking to prioritize more than they have with vaccines in the past. Some authorities think it makes sense to hold off for now on vaccinating males against HPV, even though they are, of course, the major source of infection for females. But since the majority of females pick up HPV by the time they reach their late 20s or early 30s and are therefore at risk for cervical cancer, how can we justify *not* vaccinating every girl in America?

At last year's meeting of the Interscience Conference on Antimicrobials and Chemotherapy, data were presented for a monovalent version of the current Merck vaccine containing only strain 16. In that phase II "proof of principle" study involving 1,533 women aged 16-23 years who were initially negative for HPV 16 DNA and antibodies, the vaccine was 94% effective in preventing persistent HPV infection and 100% effective against cervical intraepithelial neoplasia grades 2 and 3, compared with placebo over 3.5 years.

No cases of cervical intraepithelial neoplasia (CIN) were seen among vaccine recipients, compared with CIN 1 in 12 in the placebo group, CIN 2 in 7, and CIN 3 in 6 in the placebo group (PEDIATRIC NEWS, December 2004, p. 10).

Now, phase III data for the current quadrivalent Merck vaccine from a total of 1,529 male and female subjects aged 10-23 show 100% seroconversion at 6 months for HPV types 16, 6, and 11, and 99.9% seroconversion for serotype 18. Antibody levels for all four serotypes were significantly higher among females and males aged 10-15 years than among those aged 16-23. These data were presented earlier this year at the annual meeting of the European Society of Pediatric Infectious Diseases.

The GlaxoSmithKline vaccine also was found highly effective in a multinational randomized, placebo-controlled study of 1,113 women aged 15-25 years who were followed up to 27 months. Vaccine efficacy overall was 91.6% against incident infection and 100% against persistent infection with HPV 16 and/or 18. In the intention-to-treat analysis, vaccine efficacy was 95.1% against persistent cervical infection and 92.9% against cytologic abnormalities associated with HPV 16 and 18 infection (Lancet 2004;364:1731-2).

Merck and GlaxoSmithKline are now each studying the efficacy and safety of their HPV vaccines in more than 20,000 people aged 9-24 years. The results should tell us whether the vaccines have a therapeutic effect in women who are already infected with HPV, perhaps by inducing antibodies to generate an immune response thereby preventing the progression from simple, transient infection to persistent infection to stage 3 (CIN). However, the first order of business is to target girls before they become sexually active.

About a million women per year have an abnormal Pap smear. What follows is a series of costly and anxiety-provoking steps, including colposcopy, cervical scraping, and if abnormal cells are found, cervical biopsy and possible hysterectomy, all at a cost of approximately $2.8 billion. Widespread vaccination against HPV could substantially reduce this burden.

Although the HPV vaccines will not be the first to prevent cancer—the hepatitis B vaccine reduces the likelihood of developing hepatocellular carcinoma—they are the first to be specifically developed and marketed for cancer prevention. As an infectious disease specialist, I see this concept as novel and very, very exciting. ■

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